Applicant: Scott C. Mayer Serial No.: 10/692,874 Filed: October 24, 2003

Page : 2 of 16

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

- 1. (Canceled)
- 2. (Canceled)
- 3. (Canceled)
- 4. (Canceled)
- 5. (Currently Amended) A method of treating or inhibiting hyperproliferative vascular disorders in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of formula I having the structure

wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, trifluoromethylacyl of 3-8 carbon atoms, benzoyl, or -SO₃H;

Applicant: Scott C. Mayer Serial No.: 10/692,874 Filed: October 24, 2003

Page : 3 of 16

R⁹ is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, or alkoxy of 1-6 carbon atoms; R¹⁰ is hydrogen, -NO₂, -NHR¹¹, -NHR¹³, -N(R¹³)₂, -NCH₃R¹³, -NHCO₂alkyl, wherein the alkyl moiety contains 1-6 carbon atoms, alkylsulfonamide of 1 to 4 carbon atoms,

$$- \left\{-NH\right\} - \left\{$$

Z is O or S;

 R^{11} is an α -amino acid in which the α carboxyl group forms an amide with the nitrogen of R^{10} , wherein if said amino acid is glutamic acid or aspartic acid, the non- α carboxylic acid is an alkyl ester in which the alkyl moiety contains from 1-6 carbon atoms;

R¹² is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, <u>or</u> acyl of 2-7 carbon atoms, or benzoyl;

R¹³ is hydrogen, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, or trifluoromethylacyl of 3-8 carbon atoms, or benzoyl;

or a pharmaceutically acceptable salt thereof.

6. (Currently Amended) A method of treating or inhibiting restenosis in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of formula I having the structure

Serial No. : 10/692,874
Filed : October 24, 2003

Page : 4 of 16

wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, trifluoromethylacyl of 3-8 carbon atoms, benzoyl, or -SO₃H;

R⁹ is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, or alkoxy of 1-6 carbon atoms; R¹⁰ is hydrogen, -NO₂, -NHR¹¹, -NHR¹³, -N(R¹³)₂, -NCH₃R¹³, -NHCO₂alkyl, wherein the alkyl moiety contains 1-6 carbon atoms, alkylsulfonamide of 1 to 4 carbon atoms,

$$- \left\{-NH\right\} - \left\{$$

Z is O or S;

- R^{11} is an α -amino acid in which the α carboxyl group forms an amide with the nitrogen of R^{10} , wherein if said amino acid is glutamic acid or aspartic acid, the non- α carboxylic acid is an alkyl ester in which the alkyl moiety contains from 1-6 carbon atoms;
- R¹² is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, <u>or</u> acyl of 2-7 carbon atoms, <u>or benzoyl</u>;
- R¹³ is hydrogen, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, or trifluoromethylacyl of 3-8 carbon atoms, or benzoyl;

or a pharmaceutically acceptable salt thereof.

7. (Original) The method according to claim 6, wherein the restenosis results from a vascular angioplasty procedure, vascular reconstructive surgery, or organ or tissue transplantation.

Applicant: Scott C. Mayer Serial No.: 10/692,874 Filed: October 24, 2003

Page : 5 of 16

8. (Currently Amended) A method of inhibiting angiogenesis in a malignant tumor, sarcoma, or neoplastic tissue in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of formula I having the structure

wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, trifluoromethylacyl of 3-8 carbon atoms, benzoyl, or -SO₃H;

R⁹ is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, or alkoxy of 1-6 carbon atoms; R¹⁰ is hydrogen, -NO₂, -NHR¹¹, -NHR¹³, -N(R¹³)₂, -NCH₃R¹³, -NHCO₂alkyl, wherein the alkyl moiety contains 1-6 carbon atoms, alkylsulfonamide of 1 to 4 carbon atoms,

$$- \left\{-NH\right\} - \left\{$$

Z is O or S;

R¹¹ is an α-amino acid in which the α carboxyl group forms an amide with the nitrogen of R¹⁰, wherein if said amino acid is glutamic acid or aspartic acid, the non-α carboxylic acid is an alkyl ester in which the alkyl moiety contains from 1-6 carbon atoms;

R¹² is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, <u>or</u> acyl of 2-7 carbon atoms, or benzoyl;

Applicant: Scott C. Mayer Serial No.: 10/692,874 Filed: October 24, 2003

Page : 6 of 16

R¹³ is hydrogen, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, or trifluoromethylacyl of 3-8 carbon atoms, or benzoyl;

or a pharmaceutically acceptable salt thereof.

9. (New) A method of preventing hyperproliferative vascular disorders following vascular reconstructive surgery or transplantation in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of formula I having the structure

wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, trifluoromethylacyl of 3-8 carbon atoms, or -SO₃H;

R⁹ is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, or alkoxy of 1-6 carbon atoms; R¹⁰ is hydrogen, -NO₂, -NHR¹¹, -NHR¹³, -N(R¹³)₂, -NCH₃R¹³, -NHCO₂alkyl, wherein the alkyl moiety contains 1-6 carbon atoms, alkylsulfonamide of 1 to 4 carbon atoms,

$$-\frac{1}{2}-NH$$

Z is O or S;

Serial No. : 10/692,874

Filed : October 24, 2003

Page : 7 of 16

 R^{11} is an α -amino acid in which the α carboxyl group forms an amide with the nitrogen of R^{10} , wherein if said amino acid is glutamic acid or aspartic acid, the non- α carboxylic acid is an alkyl ester in which the alkyl moiety contains from 1-6 carbon atoms;

- R¹² is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, or acyl of 2-7 carbon atoms;
- R¹³ is hydrogen, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, or trifluoromethylacyl of 3-8 carbon atoms; or a pharmaceutically acceptable salt thereof.
- 10. (New) A method of preventing restenosis following vascular reconstructive surgery or transplantation in a mammal in need thereof, which comprises administering to said mammal an effective amount of a compound of formula I having the structure

wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, trifluoromethylacyl of 3-8 carbon atoms, or -SO₃H;

R⁹ is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, or alkoxy of 1-6 carbon atoms; R¹⁰ is hydrogen, -NO₂, -NHR¹¹, -NHR¹³, -N(R¹³)₂, -NCH₃R¹³, -NHCO₂alkyl, wherein the alkyl moiety contains 1-6 carbon atoms, alkylsulfonamide of 1 to 4 carbon atoms,

Serial No.: 10/692,874
Filed: October 24, 2003

Page : 8 of 16

$$-\frac{1}{2}-NH$$
 $-\frac{1}{2}$ $-\frac{1}{2}-NH$ $-\frac{1}{2}$ $-\frac{1}{2}-NH$ $-\frac{1}{2}$ $-\frac{1}{2}$ $-\frac{1}{2}$ $-\frac{1}{2}$

Z is O or S;

 R^{11} is an α -amino acid in which the α carboxyl group forms an amide with the nitrogen of R^{10} , wherein if said amino acid is glutamic acid or aspartic acid, the non- α carboxylic acid is an alkyl ester in which the alkyl moiety contains from 1-6 carbon atoms;

R¹² is hydrogen, CN, NO₂, halo, CF₃, alkyl of 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, or acyl of 2-7 carbon atoms;

R¹³ is hydrogen, acyl of 2-7 carbon atoms, haloacyl of 2-7 carbon atoms, nitroacyl of 2-7 carbon atoms, cyanoacyl of 2-7 carbon atoms, or trifluoromethylacyl of 3-8 carbon atoms; or a pharmaceutically acceptable salt thereof.

- 11. (New) The method according to claim 10, wherein the vascular reconstructive surgery or transplantation is vascular angioplasty procedure; vascular reconstructive surgery; or organ or tissue transplantation.
- 12. (New) The method according to claim 5, wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are each, independently, acyl of 2-7 carbon atoms or -SO₃H; Z is O;

or a pharmaceutically acceptable salt thereof.

13. (New) The method according to claim 5, wherein

 R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are each, independently, acetyl or -SO₃H;

 R^{10} is hydrogen, -NO₂, -NHR¹³, -N(R¹³)₂,

R¹³ is hydrogen, or acyl of 2-7 carbon atoms;

Serial No.: 10/692,874 Filed: October 24, 2003

Page : 9 of 16

14. (New) The method according to claim 5, which the compound of formula I is:

- a) N-Benzyl-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
- b) N-Benzyl-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof;
- c) N-(4-Nitro-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
- d) N-(4-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
- e) N-(3-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
- f) N-[3-(Acetylamino)-benzyl]-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof; or
- g) N-[3-(Acetylamino)-benzyl]-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof.
- 15. (New) The method of claim 5, wherein the method comprises administering the compound of formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutical carrier.
- 16. (New) The method according to claim 6, wherein

Serial No.: 10/692,874
Filed: October 24, 2003

Page : 10 of 16

 R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are each, independently, acyl of 2-7 carbon atoms or -SO₃H; Z is O;

or a pharmaceutically acceptable salt thereof.

- 17. (New) The method according to claim 6, wherein
- R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acetyl or -SO₃H;

 R^{10} is hydrogen, -NO₂, -NHR¹³, -N(R¹³)₂,

R¹³ is hydrogen, or acyl of 2-7 carbon atoms;

- 18. (New) The method according to claim 6, which the compound of formula I is:
 - a) N-Benzyl-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
 - b) N-Benzyl-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof;
 - c) N-(4-Nitro-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
 - d) N-(4-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
 - e) N-(3-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
 - f) N-[3-(Acetylamino)-benzyl]-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof; or

Serial No. : 10/692,874
Filed : October 24, 2003

Page : 11 of 16

g) N-[3-(Acetylamino)-benzyl]-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof.

- 19. (New) The method of claim 6, wherein the method comprises administering the compound of formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutical carrier.
- 20. (New) The method according to claim 8, wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acyl of 2-7 carbon atoms or -SO₃H;

Z is O;

or a pharmaceutically acceptable salt thereof.

21. (New) The method according to claim 8, wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acetyl or -SO₃H;

 R^{10} is hydrogen, -NO₂, -NHR¹³, -N(R¹³)₂,

R¹³ is hydrogen, or acyl of 2-7 carbon atoms;

- 22. (New) The method according to claim 8, which the compound of formula I is:
 - a) N-Benzyl-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
 - b) N-Benzyl-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof;
 - c) N-(4-Nitro-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;

Serial No.: 10/692,874 Filed: October 24, 2003

Page : 12 of 16

d) N-(4-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;

- e) N-(3-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
- f) N-[3-(Acetylamino)-benzyl]-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof; or
- g) N-[3-(Acetylamino)-benzyl]-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof.
- 23. (New) The method of claim 8, wherein the method comprises administering the compound of formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutical carrier.
- 24. (New) The method according to claim 9, wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acyl of 2-7 carbon atoms or -SO₃H;

Z is O;

or a pharmaceutically acceptable salt thereof.

25. (New) The method according to claim 9, wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acetyl or -SO₃H;

 R^{10} is hydrogen, -NO₂, -NHR¹³, -N(R¹³)₂,

R¹³ is hydrogen, or acyl of 2-7 carbon atoms;

Serial No.: 10/692,874 Filed: October 24, 2003

Page : 13 of 16

26. (New) The method according to claim 9, which the compound of formula I is:

- a) N-Benzyl-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
- b) N-Benzyl-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof;
- c) N-(4-Nitro-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
- d) N-(4-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
- e) N-(3-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
- f) N-[3-(Acetylamino)-benzyl]-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof; or
- g) N-[3-(Acetylamino)-benzyl]-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof.
- 27. (New) The method of claim 9, wherein the method comprises administering the compound of formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutical carrier.

Serial No.: 10/692,874 Filed: October 24, 2003

Page : 14 of 16

28. (New) The method according to claim 10, wherein

 R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are each, independently, acyl of 2-7 carbon atoms or -SO₃H; Z is O;

or a pharmaceutically acceptable salt thereof.

29. (New) The method according to claim 10, wherein

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, and R⁸ are each, independently, acetyl or -SO₃H;

 R^{10} is hydrogen, -NO₂, -NHR¹³, -N(R¹³)₂,

R¹³ is hydrogen, or acyl of 2-7 carbon atoms;

- 30. (New) The method according to claim 10, which the compound of formula I is:
 - a) N-Benzyl-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
 - b) N-Benzyl-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof;
 - c) N-(4-Nitro-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
 - d) N-(4-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;
 - e) N-(3-Amino-benzyl)-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof;

Serial No.: 10/692,874 Filed: October 24, 2003

Page : 15 of 16

f) N-[3-(Acetylamino)-benzyl]-octa-O-acetyl-lactobionamide or a pharmaceutically acceptable salt thereof; or

- g) N-[3-(Acetylamino)-benzyl]-octa-O-sulfo-lactobionamide or a pharmaceutically acceptable salt thereof.
- 31. (New) The method of claim 10, wherein the method comprises administering the compound of formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutical carrier.